Journal of Surgical Oncology 1999;70:247–250

Adrenal Incidentaloma: Report of 33 Cases

NESLIHAN BAŞÇIL TÜTÜNCÜ MD,* AND OLCAY GEDIK, MD
Department of Endocrinology, Hacettepe University Faculty of Medicine, Ankara, Turkey

Background and Objectives: The aim of our study was to review the imaging characteristics, endocrinologic screening and histologic diagnoses of adrenal incidentaloma cases encountered in our institute.
Methods: Thirty-three adrenal incidentaloma cases that had been evaluated in Hacettepe University Hospital between 1985 and 1995 were reviewed retrospectively. Adrenal masses were discovered incidentally by abdominal ultrasonography (USG) and/or computed tomography (CT). Detailed endocrine evaluation was carried out to rule out a possible functioning mass.
Results: Among these incidentaloma cases, 2 silent Cushing syndrome (6.06%) cases, 6 silent pheochromocytoma (18.18%) cases, 2 adrenocortical carcinoma (6.06%) cases, and 2 metastatic masses (6.06%) were diagnosed.
Conclusions: An optimal diagnostic approach to an adrenal incidentaloma would consider the results of the biochemical tests and a review of anatomical qualities depicted on CT or magnetic resonance imaging (MRI) while taking into account the previous clinical epidemiologic data.
J. Surg. Oncol. 1999;70:247–250.

KEY WORDS: **adrenal mass; silent pheochromocytoma; preclinic Cushing syndrome**

INTRODUCTION

The term "incidentaloma" refers to an adrenal mass occasionally and unexpectedly discovered during a radiological or surgical abdominal exploration for problems unrelated to adrenal function. Masses discovered during the staging of a malignant disease and thought to be metastatic are not considered incidentalomas [1]. The prevalence of adrenal incidentalomas ranges from 0.6 to 1.8% in the course of abdominal tomography [2] and about 8.7% in unselected autopsy series [1,2].

There are different algorithms for the evaluation of patients with adrenal incidentalomas. The main consideration is to rule out a hormonally active adrenal mass and a malignant lesion. Simple adrenal cysts, myelolipomas, and adrenal hemorrhages can usually be identified by their tomographic characteristics alone [1,2]. The characteristics of an adrenal mass on computed tomography (CT) or magnetic resonance imaging (MRI) may be helpful in distinguishing between benign and malignant lesions. The size of the mass is the most widely used discriminant of its benign and malignant nature, but the cutoff size below which silent adrenal incidentalomas can be safely presumed to be benign has not been clarified [1].

There exists a need to accumulate better and detailed information related to adrenal incidentaloma cases to establish more reliable guidelines for patient management. Here we report 33 adrenal incidentaloma cases that we analyzed retrospectively. The aim of our study was to review the imaging characteristics, endocrinologic screening, and histologic diagnoses of adrenal incidentaloma cases encountered in our institute.

MATERIALS AND METHODS

Since 1985, 33 adrenal incidentaloma cases have been reevaluated retrospectively from Hacettepe University Hospital archives (18 females, 15 males; ages 23–79 years). All adrenal masses were discovered incidentally

*Correspondence to: Neslihan Başçil Tütüncü, MD, Sancak Mahallesi 221. Sokak, 5/10, Yildiz 06550, Ankara, Turkey.
E-mail: tt04-k@tr-net.net.tr
Accepted 3 December 1998

by abdominal ultrasonography (USG) and CT scan. Diagnostic procedures were set up for extraadrenal complaints. None of the patients showed signs of overt adrenal dysfunction on physical examination.

Endocrine evaluation consisted of (1) measurement of serum adrenocorticotrophic hormone (ACTH) and cortisol in blood samples drawn at 2 time points (08:00 and 23:00 hr); (2) overnight dexamethasone screening test for Cushing syndrome (1 mg orally at 23:00 hr and measurement of serum cortisol at 08:00 hr the following morning); (3) measurement of 24 hr urinary excretion of vanillylmandelic acid (VMA), metanephrine (MN), and normetanephrine (NMN); (4) measurement of plasma renin activity (PRA) and aldosterone levels in supine and orthostatic posture; and (5) measurement of serum dehydroepiandrosterone sulfate (DHEA-S) at 08:00 hr.

The circadian rhythm of serum cortisol was evaluated with blood sampling at 08:00 and 23:00 hr and the percent ratio between serum cortisol levels was calculated. Adequate dexamethasone suppression was demonstrated when morning cortisol fell below 5 μg/dl (140 nmol/l). All hormone assays were performed in the same laboratory.

RESULTS

The mean age of the patients was 50.9 years (range 23–79 years). The dimensions of the masses (longest diameter considered) on CT ranged from 10 to 200 mm (mean 51.5 ± 40.4 mm). A close correlation was observed in respect to the size between CT and USG measurements in patients who underwent both imaging procedures. Twenty-nine patients underwent surgical removal of their adrenal masses. USG-guided fine-needle aspiration (FNA) biopsy was performed in 4 cases. The cytological diagnosis of 1 case was malignant epithelial carcinoma and the other 3 cases could not be diagnosed by FNA as the aspirates were non-diagnostic. Five patients were followed up with serial adrenal CT every 6 months. The dimensions of the masses did not increase and were non-functional during the follow-up visits. One patient having silent Cushing syndrome and tomographic findings of bilateral nodular adrenal hyperplasia was operated on without consultation with endocrinologists and now is being followed with the diagnosis of Nelson syndrome.

Endocrinologic screening for pheochromocytoma was carried out in all 33 patients. Of these 33 cases, 4 revealed increased 24 hr urine VMA and MN + NMN levels. After removal of the masses, the pathologic evaluation confirmed the diagnosis of pheochromocytoma. Although the endocrinologic evaluation of 2 patients revealed non-functional adrenal masses, they were surgically removed due to large dimensions (50 × 40 and 150 × 200 mm, respectively). The final pathologic diagnosis was pheochromocytoma in both patients.

TABLE I. Histologic Diagnosis of Adrenal Incidentaloma Cases With Sizes Larger Than 40 mm

Case no.	Size (mm)	Histologic diagnosis
1	83 × 77	Adrenocortical carcinoma
2	60 × 60	Adrenocortical adenoma; Cushing
3	78 × 59	Pheochromocytoma
6	45 × 48	Pheochromocytoma
7	50 × 40	Pheochromocytoma
8	56 × 57	Pheochromocytoma
9	65 × 50	Myelolipoma
15	98 × 92	Retroperitoneal fibrosis
19	50 × 40	Ganglioneuroma
20	70 × 120	Angiomyelolipoma
23	123 × 115	Malignant epithelial carcinoma
25	150 × 200	Extraadrenal pheochromocytoma
29	42 × 46	Myelolipoma
30	75 × 70	Pheochromocytoma
33	43 × 46	Adrenocortical carcinoma

Among the adrenal incidentaloma cases, 7 were diagnosed histologically as adrenocortical adenomas. Two of these cases revealed silent Cushing syndrome with endocrinologic screening. One of the non-functioning adrenocortical adenoma cases was operated on because of the heterogenic echo pattern of the mass on USG, and the other 4 cases of non-functioning adrenocortical adenoma were operated on by related surgical departments without consultation with endocrinologists. None of the non-functioning adrenocortical adenoma cases revealed hypocortisolism postoperatively and none was given corticosteroid replacement.

Table I lists the final histologic diagnoses and radiologic dimensions of 15 adrenal incidentaloma cases with sizes ⩾40 mm. Two of these cases were diagnosed to be adrenocortical carcinoma. One patient was diagnosed to be Cushing syndrome with endocrinologic screening and was operated on with the final diagnosis of adrenocortical adenoma. Cases 3, 6, 7, 8, 25, and 30 were silent pheochromocytoma cases, of which endocrinologic screening of cases 7 and 25 was non-diagnostic. Four of the adrenal incidentaloma cases were operated on because of their huge size (cases 9, 15, 20, 29); the pathologic diagnoses were myelolipoma, retroperitoneal fibrosis, angiomyelolipoma, and myelolipoma, respectively.

Table II lists the adrenal incidentaloma cases that were operated on because of the radiologic characteristics indicative of malignancy. The masses of cases 14 and 28 were both smaller than 40 mm (20 × 20 and 30 × 30 mm, respectively), and the tomographic evaluation revealed heterogenic density with necrotic and calcified areas in both masses. Histologic diagnosis revealed metastatic adenocarcinoma for case 14 and undifferentiated metastatic carcinoma for case 28.

DISCUSSION

The improvement of cross-sectional imaging techniques has dramatically increased the prevalence of adre-

TABLE II. Dimensions of the Adrenal Incidentaloma Cases With Radiologic Malignancy Criteria and Histologically Proven Malignancy

Case no.	Size (mm)	Histologic diagnosis
1	83 × 77	Adrenocortical carcinoma
14	20 × 20	Adenocarcinoma (primary?)
28	30 × 30	Undifferentiated metastatic carcinoma
33	43 × 46	Adrenocortical carcinoma

nal incidentaloma cases [3]. Thus adrenal incidentalomas are becoming a potential medical problem concerning their management. Surgery is the treatment of choice for primary malignant adrenal incidentalomas and endocrine functioning tumors [4–6]. Biochemical evaluation of the patient with an incidentally discovered adrenal mass must be performed with knowledge of the potential etiologies of the mass and the probability of a clinically silent mass exhibiting hormonal hypersecretion. The estimated chances of pheochromocytoma, aldosteronoma, glucocorticoid adenoma, and adrenal cortical carcinoma presenting as an incidentally discovered adrenal mass are, respectively, 6,500, 7,000, 35, and 58 per 100,000 patients with an adrenal mass [5].

Exhaustive endocrine evaluation is needed to exclude with certainty the diagnosis of a hormone secreting tumor. In our series, 2 of the pheochromocytoma cases presenting as an adrenal incidentaloma (cases 7 and 25) revealed normal 24 hr urine catecholamine metabolites. Patients were operated on because of the huge size of the tumors ($\geqslant$40 mm). Sensitivity of urinary VMA determination to detect pheochromocytoma is about 75%, while specificity is about 95%. Decreased renal excretory function and decreased urine acidity will also reduce urinary catecholamine metabolite levels [7]. When hypertension is only paroxysmal, measurements of catecholamines and their metabolites in plasma and urine may be normal during normotensive periods [7]. The prevalence of pheochromocytoma in the normal population is about 0.13% and is about 6.5% in an adrenal incidentaloma case [1]. The prevalence of silent pheochromocytoma is about 18.18% (6/33) in our series.

The majority of adrenal incidentaloma cases have been shown to be stable and slowly growing adrenocortical adenomas [6]. These masses that arise from the adrenal cortex may be truly non-hypersecretory or nonfunctional, but may subtly hypersecrete hormones without producing obvious clinical symptoms. Clearly, identification of a hypersecreting, hormonally active neoplasm should prompt early consideration of adrenalectomy and would not pose a significant clinical decision making dilemma [5]. Among the adrenocortical adenoma cases, we could analyze 5 cases in respect to the adrenocortical functions. Two silent Cushing syndrome cases were diagnosed (2/33; 6.06%).

The prevalence of adrenocortical carcinoma in the general population is 2 per million [3]. It is 0.05–0.2% of all cancers [3]. Although most of the adrenocortical carcinoma cases are larger than 3 cm, there are reports of cases with 1 cm diameter [3,5]. It is known that adrenocortical adenomas are usually (92%) less than 6 cm in diameter, but it was documented that 0.025% of adrenocortical adenomas were larger than 6 cm in one series [2]. The negative predictive value of a mass less than 6 cm for adrenocortical carcinoma is about 99.9% [2]. In our series, we have 2 cases of adrenocortical carcinoma with diameters of 83 and 46 mm, respectively. We also have 2 cases of metastatic masses with dimensions of 20 and 30 mm. It can be suggested that only size as a parameter would not be sufficient as a discriminant for malignancy [5,8]. Adrenal glands are one of the most common sites of metastasis, with lung and breast carcinoma metastases to adrenals in 27–30% of cases detected on autopsy [3, 9–11].

Among 14 cases of adrenal masses with dimensions $\geqslant$40 mm, 4 of them (28.57%; 4/14) revealed benign mesenchymal tumor. Six of the cases (42.86%; 6/14) were pheochromocytoma cases. We report only 1 adrenocortical adenoma with a maximum size of 60 mm.

CONCLUSIONS

The retrospective analysis of the data of 33 adrenal incidentaloma cases revealed 2 silent Cushing syndrome (6.06%; 2/33), 6 silent pheochromocytoma cases (18.18%; 6/33), 2 adrenocortical carcinomas (6.06%; 2/33), 5 non-functioning adrenocortical adenomas (15.15%; 5/33), 2 metastatic masses (6.06%; 2/33), and 7 soft tissue neoplasms (21.21%; 7/33). An optimal diagnostic approach to an adrenal incidentaloma case would consider first the results of the biochemical tests and a review of anatomical qualities depicted on CT or MRI in a multidisciplinary fashion including endocrinologists, radiologists, and surgeons. Evaluation should also take into account the clinical epidemiologic data as well as historical and physical findings.

REFERENCES

1. Osella G, Terzolo M, Borretta G, et al.: Endocrine evaluation of incidentally discovered adrenal masses (incidentalomas). J Clin Endocrinol Metab 1994;79:1532–1539.
2. Ross NS, Aron DC: Hormonal evaluation of the patient with an incidentally discovered adrenal mass. N Engl J Med 1990;323: 1401–1405.
3. Dunnick NR: Adrenal imaging: Current status. Am J Radiol 1990; 154:927–936.
4. Latronico AC, Chrousos GP: Extensive personal experience: Adrenocortical tumors. J Clin Endocrinol Metab 1997;82:1317–1324.
5. Gross MD, Shapiro B: Clinically silent adrenal masses. J Clin Endocrinol Metab 1993;77:885–888.
6. Reincke M, Nieke J, Krestin GP, et al.: Preclinical Cushing's

syndrome in adrenal "incidentalomas": Comparison with adrenal Cushing's syndrome. J Clin Endocrinol Metab 1992;75:826–832.
7. Manger WM, Gifford RW Jr: Pheochromocytoma: Current diagnosis and treatment. Cleveland Clin J Med 1993;60:365–378.
8. Bertagna C, Orth DN: Clinical and laboratory findings and results of therapy in 58 patients with adrenocortical tumors admitted to a single medical center (1951–1978). Am J Med 1981;71:855–875.
9. Gross MD, Shapiro B, Bouffard A, et al.: Distinguishing benign from malignant euadrenal masses. Ann Intern Med 1988;109:613–618.
10. VanErkel AR, Van Gils APG, Lequin M, et al.: CT and MR distinction of adenomas and nonadenomas of the adrenal gland. J Comput Assist Tomogr 1994;18:432–438.
11. Lee MJ, Hahn PF, Papanicolaou N, et al.: Benign and malignant adrenal masses: CT distinction with attenuation coefficients, size, and observer analysis. Radiology 1991;179:415–418.